PATENT
Docket No. 265.00230101

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Stanton et al.	Group Art Unit:	1647
Serial No.:	09/641,801	Examiner:	Christopher Nichols
Confirmation No.:	5388		
Filed:	August 17, 2000		

For: USE OF COLOSTRININ, CONSTITUENT PEPTIDES THEREOF, AND ANALOGS THEREOF FOR INDUCING CYTOKINES

AMENDMENT AND RESPONSE

Commissioner for Patents
Mail Stop Amendment
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the Office Action mailed April 29, 2004, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on the page entitled "Amendments to the Claims."

Remarks begin on the page entitled "Remarks."

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

Listing of Claims

1. **(Previously Presented)** A method of inducing a cytokine in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator consists of MQPPPLP (SEQ ID NO:1), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to SEQ ID NO:1.

2. **(Original)** The method of claim 1 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

3. **(Original)** The method of claim 1 wherein the cell is a mammalian cell.

4. **(Original)** The method of claim 3 wherein the cell is a human cell.

5. **(Canceled)**

6. **(Previously Presented)** A method for modulating an immune response in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator consists of MQPPPLP (SEQ ID NO:1), an active analog thereof, and combinations thereof, wherein the active analog

comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to SEQ ID NO:1.

7. **(Original)** The method of claim 6 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

8. **(Original)** The method of claim 6 wherein the cell is a mammalian cell.

9. **(Original)** The method of claim 8 wherein the cell is a human cell.

10. **(Canceled)**

11. **(Previously Presented)** A method for modulating an immune response in a patient, the method comprising administering to the patient an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator consists of MQPPPLP (SEQ ID NO:1), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to SEQ ID NO:1.

12. **(Canceled)**

13. **(Original)** The method of claim 11 wherein the immunological regulator is administered as part of a dietary supplement.

14. **(Original)** The method of claim 11 wherein the immunological regulator is administered topically.

15. **(Original)** The method of claim 11 wherein the patient is an animal.

16. **(Original)** The method of claim 15 wherein the patient is a human.

17. **(Original)** The method of claim 11 wherein the immune response is a specific immune response.

18. **(Original)** The method of claim 11 wherein the immune response is a nonspecific immune response.

19. **(Original)** The method of claim 11 wherein the immune response is the interferon response or antibody production.

20. **(Currently Amended)** A method for modulating leukocyte proliferation, the method comprising contacting leukocytes with a leukocyte regulator selected from the group consisting of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof, under conditions effective to change the number of leukocytes; wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to one or more constituent peptides of colostrinin, which are selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:34; and wherein the number of leukocytes is changed.

21. **(Previously Presented)** The method of claim 20 wherein the leukocytes are present in a cell culture or an organism.

22. **(Previously Presented)** The method of claim 20 wherein the leukocytes are mammalian cells.

23. **(Previously Presented)** The method of claim 22 wherein the leukocytes are human cells.

24. **(Previously Presented)** The method of claim 22 wherein the leukocytes are increased in number.

25. **(Previously Presented)** The method of claim 24 wherein the leukocytes are differentiated.

26. **(Previously Presented)** The method of claim 22 wherein the leukocyte regulator is a constituent peptide of colostrinin.

27. **(Currently Amended)** The method of claim 26 wherein the leukocyte regulator is selected from the group consisting of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLQPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), VESYVPLFP (SEQ ID NO:31), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof; wherein the active analog comprises a peptide having an amino acid sequence with at least about

15 percent proline and having at least about 70 percent sequence identity to one or more constituent peptides of colostrinin, which are selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:34.

28. **(Previously Presented)** The method of claim 27 wherein the leukocyte regulator is selected from the group consisting of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLQPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPEP (SEQ ID NO:8), YPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), and combinations thereof.

29. **(Currently Amended)** A method for modulating leukocyte proliferation in a patient, the method comprising administering to the patient a leukocyte regulator selected from the group consisting of colostrinin, a constituent peptide thereof, an analog thereof, and combinations thereof, under conditions effective to change the number of leukocytes; wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to one or more constituent peptides of colostrinin, which are selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:34; and wherein the number of leukocytes is changed.

30. **(Original)** The method of claim 29 wherein the patient is a human.

31. **(Previously Presented)** The method of claim 29 wherein the leukocytes are increased in number.

32. **(Previously Presented)** The method of claim 31 wherein the leukocytes are differentiated.

33. **(Previously Presented)** The method of claim 29 wherein the leukocyte regulator is a constituent peptide of colostrinin.

34. **(Currently Amended)** The method of claim 33 wherein the leukocyte regulator is selected from the group consisting of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLQPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), VESYVPLFP (SEQ ID NO:31), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof; wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to one or more constituent peptides of colostrinin, which are selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:34.

35. **(Previously Presented)** The method of claim 34 wherein the leukocyte regulator is selected from the group consisting of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLQPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPEP (SEQ ID NO:8),VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), and combinations thereof.

36. **(Canceled)**

37. **(Currently Amended)** A method of inducing a cytokine in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is a constituent peptide of colostrinin selected from the group consisting of LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLQPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof, wherein the active analog

comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to a one or more constituent peptides of colostrinin which are selected from the group consisting of SEQ ID NO:2-30 and 32-34.

38. **(Currently Amended)** A method for modulating an immune response in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is a constituent peptide of colostrinin selected from the group consisting of LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLQPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to one or more constituent peptides of colostrinin which are selected from the group consisting of SEQ ID NO:2-30 and 32-34.

39. **(Currently Amended)** A method for modulating an immune response in a patient, the method comprising administering to the patient an immunological regulator under conditions

effective to induce a cytokine, wherein the immunological regulator is a constituent peptide of colostrinin selected from the group consisting of LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLQPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to one or more constituent peptides of colostrinin which are selected from the group consisting of SEQ ID NO:2-30 and 32-34.

Remarks

The Office Action mailed April 29, 2004 has been received and reviewed. Claims 5, 10, 12, and 36 having been canceled, and claims 20, 27, 29, 34, and 37-39 having been amended, the pending claims are claims 1-4, 6-9, 11, 13-35, and 37-39. Reconsideration and withdrawal of the rejections are respectfully requested.

Double Patenting Rejection

Claims 1-4, 6-9, 11, 13-35, and 37-39 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,500,798. Claims 1-4, 6-9, 11, 13-35, and 27-39 were also rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent Application Serial No. 09/641,802. Submitted herewith is a Terminal Disclaimer which, Applicants submit, is in compliance with 37 CFR 1.321(c) and thereby obviates the Examiner's double patenting rejection of claims 1-4, 6-9, 11, 13-35, and 37-39

Claim Objection

In view of the amendment of claim 20 to recite "selected from the group consisting of," Applicants respectfully submit that the Examiner's objection to claim 20 is moot.

The 35 U.S.C. §102 Rejection

The Examiner rejected claims 20-35 under 35 U.S.C. §102(b) as being anticipated by Janusz et al. (*Molecular Immunology*; 24(10):1029-1031). The Examiner also rejected claims 20-35 under 35 U.S.C. §102(b) as being anticipated by Inglot et al. (*Archivum Immun Thera Exp*; 44(4):215-224). Applicants traverse the rejection of claims 20-35 as being anticipated by either Janusz et al. or Inglot et al. According to MPEP § 2131 a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

Applicants respectfully submit that neither Janusz et al. nor Inglot et al. set forth each and every element of the methods of claims 20-35. Janusz et al. teaches that the administration of the colostrinin nonapeptide NP (SEQ ID NO:31) to mice enhances the primary immune response to sheep red blood cells (SRBC) in the mice (Janusz et al., page 1030). Inglot et al. teaches that colostrinin is a "modest inducer" of the cytokines IFN and TNF in human peripheral blood leukocytes and whole blood cultures and resulted in "psycho-stimulation" when orally administered to two human patients (see Inglot et al., abstract and page 215).

Claims 20-28 are drawn to "[a] method for modulating leukocyte proliferation, the method comprising contacting leukocytes with a leukocyte regulator . . . under conditions effective to change the number of leukocytes . . . wherein the number of leukocytes is changed," while claims 29-35 are drawn to "[a] method for modulating leukocyte proliferation in a patient, the method comprising administering to the patient a leukocyte regulator . . . under conditions effective to change the number of leukocytes . . . wherein the number of leukocytes is changed." In the claimed methods for modulating leukocyte proliferation, leukocytes are contacted with a leukocyte regulator (claims 20-28) or a leukocyte regulator is administered to a patient (claims 29-35) "under conditions effective to change the number of leukocytes . . . wherein the number of leukocytes is changed." Thus, in the claimed methods a leukocyte regulator is administered *under conditions effective to change the number of leukocytes*, and *wherein the number of leukocytes is changed.* Applicants respectfully submit that the Examiner's statements that claims 20-35 "are drawn to a method which comprises the step of contacting cells with an 'immunological regulator'" and that "[n]o other limitations are present in the claims" (pages 4 and 6 of the Office Action mailed April 29, 2004) are incorrect.

Applicants submit that neither Janusz et al. nor Inglot et al. teach administering a leukocyte regulator *under conditions effective to change the number of leukocytes* or *wherein the number of leukocytes is changed.* Thus, the disclosures of Janusz et al. or Inglot et al. do not set forth each and every element of claims 20-35. Withdrawal of this rejection under 35 U.S.C. §102(b) is respectfully requested.

Summary

It is respectfully submitted that the pending claims 1-4, 6-9, 11, 13-35, and 37-39 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
Stanton et al.

By
Mueting, Raasch & Gebhardt, P.A.
P.O. Box 581415
Minneapolis, MN 55458-1415
Phone: (612) 305-1220
Facsimile: (612) 305-1228
Customer Number 26813

July 28, 2004
Date

By: Nancy A. Johnson
Nancy A. Johnson
Reg. No. 47,266
Direct Dial (612)305-4723

CERTIFICATE UNDER 37 CFR §1.10:
"Express Mail" mailing label number: EV201890414 US Date of Deposit: July 28, 2004
The undersigned hereby certifies that the Transmittal Letter and the paper(s) and/or fee(s), as described hereinabove, are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By: Sara E. Olson
Name: SARA E. OLSON